Remarks

Claims 1- 52 are pending in the application. Claims 32-52 have been withdrawn from consideration. Claims 1-31 are currently rejected. Applicants have amended claims 1, 8, 18, 19, 20, 21, 23, 30, and 31 in the current application. Claims 1, 20, 21, 23, and 31 were done to further clarify the claims and correct obvious errors within the claims. The amendments to claims 1, 18, 19, and 30 are discussed below. No new matter has been added by these claim amendments.

A. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH FOR INDEFINITENESS SHOULD BE WITHDRAWN

Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, for the reasons noted in the Office Action. Specifically, the Office Action questions whether the device of the current invention can actually modulate an immune response without the antigen being disposed within the device. Applicants submit that the device of original claim 1 in fact is suitable for use as an immune modulation device. Embodiments where an antigen is not required are set forth at page 18, lines 9-28. In one embodiment, the device is implanted, cells allowed to migrate into the device, and then the device is removed and the cells cryopreserved. The cells may then be placed back into the body, for example to replenish the patient's immune system after whole body radiation. Notwithstanding the above, Applicants have amended claim 1 and deleted claim 29, without prejudice to the presentation of that claim in a continuing application, by including an antigen to expedite prosecution on the merits with respect to embodiments including an antigen disposed within the interior lumen of the shell. Applicants respectfully submit that claims 1-28 and 30-31 are patentable under 35 U.S.C. 112 second paragraph, and request that the rejection thereof be withdrawn.

Claims 18-24 are rejected under 35 U.S.C. 112, second paragraph, for the reasons set forth in the Office Action. In particular, the Office Action alleges that it is unclear whether the entire immune modulation device can be made from the group of materials listed within claim 18, or whether the shell and scaffolding can be made of different materials. Applicants have amended claim 18 to indicate that both the shell and the scaffolding are made from a polymer as claimed in claim 18, although each may be made from a different polymer included within the Markush grouping. Claim 19 is further amended to indicate that both the shell and the

scaffolding are made from an aliphatic polyester. As indicated in Examples 1-3, the shell may be made from poly(para-dioxanone) and the fibrous scaffolding may be made from a glycolide-co-lactide polymer, each of which is an aliphatic polyester. In view of the amendment, Applicants respectfully submit that claims 18-24 are patentable under 35 U.S.C. 112, second paragraph, and request that the rejection thereof be withdrawn.

Claims 29-31 have been rejected under 35 U.S.C. second paragraph, for the reasons noted in the office action; namely, the Office action alleges that it is unclear where the antigen is retained in the claimed device. Applicants have amended claim 1 to recite that the antigen is disposed in the interior lumen of the device, and deleted claim 29. In view of the Amendment, Applicants respectfully submit that claims 30-31 are patentable under 35 U.S.C. 112, second paragraph, and request that the rejection thereof be withdrawn.

B. THE REJECTION UNDER 35 U.S.C. § 103 (a) FOR OBVIOUSNESS IN LIGHT OF CERAMI AND LI SHOULD BE WITHDRAWN

Claims 1-3, 6-10, 15-21, and 29-31 are rejected under 35 U.S.C. 103(a) over Cerami et al. (WO 99/44583) in view of Li et al. (US 6,303,136). Applicants respectfully traverse.

Applicants respectfully submit that the combination of Cerami and Li is improper, and thus the claims are patentable under 35 U.S.C. §103, because Li is nonanologous art. The present invention is directed to immune modulating devices, one embodiment of which includes an antigen disposed within the interior lumen of such a device. Li is directed to an implantable device for cell screening and implantation of cells in the body (Col. 1, ll. 13-15).

The test for determining whether a reference in the prior art is "analogous" has been set forth by the Court of Appeals for the Federal Circuit (CAFC) in In re Clay, 23 U.S.P.Q.2d 1058 (Fed. Cir., June 10, 1992). The two criteria for determining whether art is analogous are the following: 1) whether the art is from the same field of endeavor, regardless of the problem addressed, and 2) if the reference is not within the field of the inventor's endeavor, whether the reference still is reasonably pertinent to the particular problem with which the inventor is involved. See Clay at page 1058.

With respect to the first criteria, the immune modulating devices claimed by Applicants look to modulate an immune response by providing a robust, long-term immune response, or by down regulating an existing response (p.l, ll.5-10). Desired immunomodulatory responses can include either generation of humoral and/or cellular immunity against the desired antigen or, alternatively, desensitization towards particular allergen or cell types (p.15, l.35 – p.16 l. 2), depending on which

antigen is disposed within the device. This is accomplished by allowing immune cells of the body to enter the device and interact with the antigen. In essence, Applicants' devices serve as a form of vaccination against antigens.

On the other hand, Li relates to implantable devices useful for cell screening and cell implantation (Col. 1, ll. 13-15). The devices of Li prevent immune cells from entering the device to interact with, or destroy the implanted cells. Clearly, Li is not concerned with modulating immune responses within the body and therefore is not from the same field of endeavor as Applicants' invention.

With respect to the second criteria, the purposes of both the invention and the prior art are important in determining whether the reference is reasonably pertinent to the problem which the invention attempts to solve (see Clay at page 1061).

In reality, Li was interested in solving a completely different problem from that which Applicant has solved. Li was seeking to provide treatment of various conditions by way of seeding a scaffold with cells, implanting the scaffolds into the body, isolating those seeded cells from the body and then permitting molecules produced by the seeded cells to migrate from the device into the body (col. 6, ll.58-63). It is essential in Li to isolate the cells within the device to prevent contact with the body's immune system.

Conversely, Applicants seek to provide enhanced modulation of immunological response by permitting cells of the body to ingress into the device in order to interact with antigens placed within the device. Cells then may egress from the interior of the device to provide enhanced modulation of an immune response in the body, whether it be providing an immune response to an antigen, or down regulating, or desensitizing, a response to, e.g. an allergen. As such, Applicants respectfully submit that Li clearly is not pertinent to Applicants' particular problem.

In determining whether the second criteria is met, the Court in Clay also looked at whether the particular invention functions in a similar manner to that of the cited reference in question. In the instant case, cells from the body are allowed to migrate into the device, where they interact with and process antigens within the device. Cells may proliferate in the presence of the antigen(s) and egress back into the body. Such cells exhibit enhanced ability to modulate an immune response to antigens of the same nature when encountered elsewhere in the body at a later occurrence. Futhermore, such devices hinder migration of soluble molecules, e.g. cytokines, from the device, so as to provide a local concentration of cells and cytokines to

enhance the immune response relative to implantation of antigens with standard adjuvants (p. 7, ll. 16-23).

The Li devices contain a permselective membrane encapsulating a fibrous scaffold having cells seeded thereon (Col.2, ll. 29-38) and the devices functions just the opposite of Applicants' devices. On the one hand, the membrane allows biologically active molecules, e.g. cytokines and lymphokines, to migrate out of the device into the body. The membrane also, and most importantly, creates a protective barrier that prohibits the host immune system from migrating into the device to destroy the seeded cells (Col. 6, ll.34-36). Therefore, Applicants respectfully submit that the two types of devices clearly do not function in a similar manner, as is fully supported by the disclosure of Li.

In summary, Applicants respectfully submit that the use of Li as prior art is impermissible because Li clearly represents non-analogous art.

Applicants respectfully disagree with certain characterizations made by the Examiner at page 4 and 5 of the Office Action.

The Office Action maintains that the Cerami and Li devices are similar. Applicants respectfully but strongly disagree.

The Examiner states that it would be **obvious** to one skilled in the "art" to use the matrix of Li in the device of Cerami. However, Applicants would question as to which "art" is being considered; the art of immune modulating devices, or the art of implants seeded with cells?

Accordingly, Applicants respectfully submit that *a prima facie* case of obviousness has not been established. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 1-3, 6-10, 15-21, and 29-31.

Applicants respectfully submit that, even if Li is properly combined with Cerami, and Applicants respectfully submit that it is not, the combination does not render obvious claims 17-21. As noted at page 10, lines 25-36 and page 11, lines 1-5, embodiments of Applicants invention utilizing absorbable polymers for the shell and scaffolding degrade within 1-6 months upon implantation in the body. Contrary to Applicants' invention, Li requires a non-degradable, i.e. "non-bioabsorbable", fibrous scaffolding. As such, Applicants respectfully submit that Li in fact teaches away from embodiments wherein the device is bioabsorbable, as claimed in claims 17-26.

Based on all of the foregoing, Applicants respectfully submit that all pending claims are

patentable over Cerami in view of Li under 35 U.S.C. 103(a) and request that the rejection thereof be withdrawn.

C. THE REJECTION UNDER 35 U.S.C. § 103 (a) FOR OBVIOUSNESS IN LIGHT OF CERAMI, LI, AND ROTH SHOULD BE WITHDRAWN

Claims 4-5 are rejected under 35 U.S.C. 103(a) over Cerami and Li, further in view of Roth et al. (US 4,128,612). Applicants respectfully traverse.

Initially, Applicants reiterate all of the arguments as set forth above with respect to Cerami and Li and maintain that claims 4-5 are patentable on those bases alone. Furthermore, Roth is directed to absorbable surgical felt useful in providing hemostasis. Applicants respectfully submit that the structure of felt pads for providing hemostasis is in no way related to a fibrous scaffolding as claimed by Applicants. As such, Applicants respectfully submit that Roth, as with Li, is non-analogous art for obvious reasons and is improperly cited. Furthermore, Applicants respectfully submit that one skilled in the art of immune modulating devices would not be motivated by Roth to utilize filaments as claimed in claims 4-5. Again, it is respectfully submitted that hindsight selection has been used to construct the rejection of claims 4-5. Accordingly, Applicants respectfully submit that claims 4-5 are patentable under 35 U.S.C. 103(a) over Cerami and Li, further in view of Roth and request that the rejection thereof be withdrawn.

D. THE REJECTION UNDER 35 U.S.C. § 103 (a) FOR OBVIOUSNESS IN LIGHT OF CERAMI, LI, AND KENNEDY SHOULD BE WITHDRAWN

Claims 11-14 are rejected under 35 U.S.C. 103(a) over Cerami and Li, further in view of Kennedy at al. (US 6,200,589). Applicants respectfully traverse.

Initially, Applicants reiterate all of the arguments as set forth above with respect to Cerami and Li and maintain that claims 11-14 are patentable on those bases alone. In addition, Kennedy relates to an implantable device with a semi-permeable membrane for purposes of providing an immunoisolating enclosure for implanted cells. Therefore, Applicants respectfully submit that Kennedy, like Li, is non-analogous art and improperly cited in that it does not relate to immune modulating devices. Furthermore, it is respectfully submitted that hindsight selection

has been used to construct the rejection of claims 11-14. Accordingly, Applicants respectfully submit that claims 11-14 are patentable under 35 U.S .C. 103(a) over Cerami and Li, further in view of Kennedy and request that the rejection thereof be withdrawn.

E. THE REJECTION UNDER 35 U.S.C. § 103 (a) FOR OBVIOUSNESS IN LIGHT OF CERAMI, LI AND BEZWADA SHOULD BE WITHDRAWN

Claims 22-24 are rejected under 35 U.S.C. 103(a) over Cerami and Li, further in view of Bezwada et al. (US 5,597,579). Applicants respectfully traverse.

Initially, Applicants reiterate all of the arguments as set forth above with respect to Cerami and Li and maintain that claims 22-24 are patentable on those bases alone. Claims 22-24 are directed to a bioabsorbable device where both the shell and fibrous scaffold are made from a bioabsorbable aliphatic polyester. As Li requires the use of a nonabsorbable fibrous matrix, Applicants respectfully submit that the combination of Cerami, Li and Bezwada does not meet the limitations of claims 22-24. Accordingly, Applicants respectfully submit that claims 22-24 are patentable under 35 U.S.C. 103(a) over Cerami and Li, further in view of Bezwada and request that the rejection thereof be withdrawn.

F. THE REJECTION UNDER 35 U.S.C. § 103 (a) FOR OBVIOUSNESS IN LIGHT OF CERAMI, LI, BEZWADA AND DASCH SHOULD BE WITHDRAWN

Claims 25-26 are rejected under 35 U.S.C. 103(a) over Cerami, Li, and Bezwada further in view of Dasch et al. (US 2003/0236192). Applicants respectfully traverse.

Initially, Applicants reiterate all of the arguments as set forth above with respect to Cerami and Li and their further combination with Bezwada. Applicants also maintain that claims 25-26 are patentable on those bases alone. Further, the disclosure of Dasch relates to sustained release compositions for the delivery of therapeutic agents and therefore is not analogous to the current art. *See* Dasch, abstract. Accordingly, Applicants respectfully submit that claims 25-26 are patentable under 35 U.S.C. 103(a) over Cerami, Li, and Bezwada further in view of Dasch and request that the rejection thereof be withdrawn.

G. THE REJECTION UNDER 35 U.S.C. § 103 (a) FOR OBVIOUSNESS IN LIGHT OF CERAMI, LI, BEZWADA, DASCH AND BEZWADA ('997) SHOULD BE WITHDRAWN

Claims 27 and 28 are rejected under 35 U.S.C. 103(a) over Cerami, Li, Bezwada, and Dasch further in view of Bezwada (US 5,951,997). Applicants respectfully traverse.

Initially, Applicants reiterate all of the arguments as set forth above with respect to Cerami and Li and their further combination with Bezwada and Dasch. Applicants, also maintain that claims 27 and 28 are patentable on those bases alone. Bezwada '997 is directed to absorbable sutures made of aliphatic polyesters that are absorbable. However, Li relates to a nonabsorbable device. Thus, it would appear to Applicants that the Examiner now is intending to modify Li against the express teaching of Li that requires nondegradable fibers, by substituting the nondegradable, nonabsorbable fibers required in Li, assumedly with fibers manufactured from absorbable polymers disclosed in Bezwada '997. Applicants respectfully submit that this, again, is impermissible hindsight selection.

Accordingly, Applicants respectfully submit that claims 27 and 28 are patentable under 35 U.S.C. 103(a) over Cerami, Li, Bezwada, and Dasch further in view of Bezwada '997 and request that the rejection thereof be withdrawn

H. THE REJECTIONS FOR NONSTATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING SHOULD BE WITHDRAWN

Claims 1-31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 6,958,158 ('158 patent), for the reasons noted in the Office Action.

In response, and without agreeing with the double patenting rejection, Applicants intend to submit an appropriate Terminal Disclaimer once the claims are indicated to be allowable in the present application but for a Terminal Disclaimer. In the meanwhile, Applicants request that these double patenting rejections be held in abeyance.

Additionally, 1, 2, 7, 8, and 16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-4, 8-12, 22 and 23 of Application No.

10/364,030 ('030), for the reasons noted in the Office Action. Applicants assert that the amendment to claim 1 indicating that an antigen is disposed on the interior lumen of the immune modulation device obviates the obviousness-type double patenting rejection. The Office Action alleges the '030 application recites a mammalian cell type other than an immune cell seeded on the scaffolding. However, amended claim 1 of the present application currently recites that an antigen is disposed within the lumen of the device. An antigen is an immune related compound and therefore, according to the Examiner, is expressly excluded under the '030 application. Thus, the claims 1, 2, 7, 8, and 16 would not be obvious in light of the '030 application.

Conclusion

Applicants respectfully submit that this is a complete response to the Office Action and that all pending claims are patentable. Accordingly, Applicants respectfully request a notice of allowance to that affect. Applicants would welcome a telephonic interview with the Examiner upon entry of the Amendment to discuss the Amendment and arguments set forth herein.

Respectfully submitted,

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By: Fred J. Hamble 42,623
Frederick J. Hamble (Reg. No.)

712 Kitchawan Road
Ossining, NY 10562
(914) 762-7586